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(54) Sensors for the determination of organometallic compounds

(57) Sensors for the determination of organometallic compounds, e.g. *n*-butyllithium, comprise the following elements:

a) an inorganic, organic or polymeric support, insoluble in the sample to analyze

b) an indicator which reversibly reacts with the organometallic compound and whose reaction product gives a characteristic absorption, reflection or emission band in the range 150-15000nm, e.g. 1,10-phenanthroline and derivatives, triphenylmethane, or N-[2-(4-hydroxybenzyl)phenyl]-2,2-dimethylpropanamide, and which is physically trapped, adsorbed, absorbed, dissolved or chemi-

cally linked in an electrostatic or covalent way to the support

c) an optical sensor which measures the absorption, reflection or emission of the functionalized support at the characteristic wavelength and transforms it in the concentration of the organometallic present in the solution.

Also described is the method for the determination of the concentration of organometallic compounds by the on line use of a sensor in anionic polymerizations.

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Description

FIELD OF THE INVENTION

- 5 [0001] The invention refers to sensors useful for organometallic compounds determination and to the on line spectroscopic monitorization of such reactive species, particularly in anionic polymerization initiated by organolithium compounds or any other reaction that involves an organometallic compound being critical the stoichiometry of the same.

BACKGROUND OF THE INVENTION

- 10 [0002] As described in the prior art, there are several methods for the determination of organolithium compounds.
- [0003] Kofron and Baclawski [Kofron, W.G.; Baclawski, L.M.; J. Org. Chem. 1976, 41, 1879] describe the use of diphenyl acetic acid as colorimetric indicator.
- 15 [0004] As alternatives to diphenyl acetic acid, similar indicators have been proposed. 4-biphenyl methanol, 4-biphenyl acetic acid [Juaristi, E.; Martínez-Richa, A.; García Rivera, A.; Cruz-Sánchez, J.S.; J.Org. Chem. 1983, 48, 2603], and 1-pyreneacetic acid [Kiljumen, H.; Hase, T.A.; J.Org.Chem. 1991, 56, 6950] have been used as indicator molecules for the titration of organolithium compounds providing a clearer visual detection of the equivalence point due to a more extended delocalization of the charge in the coloured final dianions.
- 20 [0005] In the same way, Winkle et al. [Winkle, M.R.; Lansinger, J.M.; Donald, R.C.; J. Chem. Soc. Chem. Commun. 1980, 87] have used 2,5-dimethoxybenzyl alcohol as indicator for the titration of organolithium reagents, resulting in the formation of visually detectable coloured dianionic species.
- [0006] More recently, new titration methods for the determination of alkyl- and aryllithium compounds based on the double deprotonation of different colorimetric indicators have been reported. This is the case of the procedure described by Suffert [Suffert, J.; J.Org.Chem. 1989, 54, 509] proposing *N*-pivaloyl-*o*-toluidine and/or *N*-pivaloyl-*o*-benzyl aniline as indicator dyes.
- 25 [0007] Another group of indicators that undergo a double deprotonation upon reacting with lithium organometallic compounds include benzenesulphonyl- and tosylhydrazone derivatives [Miranda, R.; Hernández, A.; Angeles, E.; Cabrera, A.; Salmón, M.; Joseph-Nathan, P.; Analyst, 1990, 115, 1483].
- 30 [0008] Another possibility of determining organolithium compounds by colorimetric titration is based on the single deprotonation of triphenylmethane [Eppley, R.L.; Dixon, J.A.; J. Organomet. Chem 1967, 8, 176], *N*-benzyliden-benzylamine [Duhamel, L.; Plaquevant, J.C.; J.Org.Chem. 1981, 44, 24304] or *N*-phenyl-1-naphthylamine [Bergbreiter, D. E.; Pendergrass, E.; J.Org.Chem. 1981, 46, 219] to yield, after reaction with the organolithium compound, the corresponding coloured anions that can be back-titrated with *sec*-butyl alcohol or benzoic acid solution.
- 35 [0009] Moreover, the fact that alkyl organolithium and organomagnesium compounds form coloured complexes with different Lewis bases, all of them having extended π or aromatic structure, provides us one of the more used optical methods for the titration of such organometallic compounds. The charge-transfer complexes obtained in this way display an intense absorption in the visible region of the electromagnetic spectrum. The most common polycyclic aromatic bases used to that end are 1,10-phenanthroline and 2,2-biquinoline [Watson, S.C.; Eastham, J.F.; J.Organomet.Chem. 1967, 9, 165].
- 40 [0010] On the other hand, industrial anionic polymerization initiated by organolithium compounds is one of the more versatile methods for synthesizing macromolecules due to the possibility of designing very different chemical structures for many applications, but a strict control of the process is required. Living anionic polymerization of 1,3-conjugated diene and/or monoalkenyl aromatic hydrocarbon, allows us to synthesize macromolecular compounds with a high control of their composition and structural parameters such as molecular weight distribution, microstructure, stereochemistry, branching and chain functionalization. The molecular weight of the polymer is one of the most important variables that affect the macromolecular properties. In a living anionic polymerization, the molecular weight is determined by the reaction stoichiometry and the conversion rate. This solution polymerization process is extremely sensitive to impurities in the reaction medium that can modify the effective initiator concentration or the number of growing chains. That is the reason why one of the main parameters to be controlled in such processes is the so called reaction threshold, namely, the amount of initiator consumed by impurities or "poisons" able to react with it before the initiation step is effective.
- 50 [0011] Therefore, according to the background, a method based on sensors useful for titration of organolithium compounds by spectroscopic monitorization of reactive species has not been described up to date, with particular application to anionic polymerization processes initiated by organolithium compounds or any other process that involves an organometallic compound being critical the stoichiometry of this compound.
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DETAILED DESCRIPTION OF THE INVENTION

[0012] A fiber-optic sensor is a device able to measure a physical parameter or to determine the concentration and/or activity of a chemical species "in situ", continuously and in real time, through an optical fiber, using the variation of the optical properties of a reagent phase. This sensing phase is placed in the sensitive terminal (that could be the optical fiber with an optical indicator), whose optical properties vary on contacting a chemical stimulus.

[0013] These optical sensors allow us to titrate organometallic compounds and to monitor the neutralization point of all the impurities that destroy the initiator used in the anionic polymerization of 1,3-conjugated dienes and/or monoalkenyl aromatic hydrocarbons or any other process that involves an organometallic compound being critical the stoichiometry of the same. The procedure implies a continuous, "in situ" and real-time measurement of the reaction threshold in contrast with the conventional method based on taking out and analyzing the sample that has some inherent limitations (slowness, discontinuity, manipulation required,...)

[0014] It has been found that different combinations of indicator and support can be used to design sensors for the determination of organometallic compounds.

[0015] The sensitive terminal is the most important element in the construction of a so-called chemical sensor because it contains the reactive phase or sensitive layer. This reactive phase can be located either at the distal end of the optical fiber or inserted into the cladding of the fiber core or in the evanescent wave region, replacing part of the fiber cladding. An improvement in the sensor sensitivity and/or selectivity can be achieved by confining the reactive phase using a membrane to separate it from the analyte phase or a permeable polymer as the indicator support or by covalent binding of the indicator dye to long chain polymers that improve the accessibility of the analyte.

[0016] Therefore, an object of the present invention is the provision of an optical sensor useful for the qualitative and/or quantitative determination of organometallic compounds, specially organometallic compounds wherein the metal is a metal of groups 2 and 13 of the Periodic Table of the Elements, preferably for the determination of organolithium compounds.

[0017] Another object of the present invention is the provision of an optical sensor useful for the determination of the reaction threshold in the anionic polymerization of a 1,3-conjugated diene and/or monoalkenyl aromatic hydrocarbon copolymer, namely the amount of initiator consumed by impurities or "poisons" able to react with it before the initiation step is effective or any other reaction that involves an organometallic compound being critical the stoichiometry of the same.

[0018] The sensor for the qualitative and/or quantitative determination of organometallic compounds according to the present invention comprises the following elements:

- a) an inorganic, organic or polymeric support insoluble in the sample to analyze;
- b) an indicator which reversibly reacts with the organometallic compound and whose reaction product gives a characteristic absorption, reflectance or emission band in the range 150-15000 nm, preferably 200-800 nm and which is physically entrapped, adsorbed, absorbed, dissolved or chemically bound in an electrostatic or covalent way to the support; and
- c) an optical sensor which measures the absorption, reflectance or emission of the functionalized support at the characteristic wavelength and transforms it in the concentration of the organometallic present in the solution.

[0019] The optical indicator dye, whose absorbance, reflectance or emission will change in the presence of organometallic compounds, belongs preferably to heterocyclic aromatic compounds (for example 1,10-phenanthroline, 5-amino-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 5-hydroxy-1,10-phenanthroline, sodium 1,10-phenanthroline-4,7-di(phenylsulphonate), 5-perfluorooctanamide-1,10-phenanthroline, 4-vinyl-7-methyl-1,10-phenanthroline), N-(2-methyl)-2,2-dimethylpropanamide, N-[2-(4-hydroxybenzyl) phenyl]-2,2-dimethylpropanamide, N-(2-benzylphenyl)perfluorooctanamide, N-[4-(2-(2,2-dimethylpropanoylamino)benzyl)phenyl]-perfluorooctanamide or triarylmethane derivatives (for example 4,4'-(difluorophenyl) phenylmethane and triphenylmethane).

[0020] The indicator supports can be of very different chemical composition but can be preferably classified by its inorganic (for example, silicagel, powdered porous glass, porous glass layer, poly(dimethylsiloxanes), silicic xerogels) or organic (for example, poly(tetrafluoroethylene), poly(vinyl chloride), Nafion® membranes, styrenedivinylbenzene copolymers) nature.

[0021] The preferred immobilization procedures are adsorption for poly(tetrafluoroethylene) [Blair, T.L.; Cynkowski, T.; Bachas, L.G.; Anal.Chem. 1993, 65, 945] and Nafion® [García-Fresnadillo, D.; Marazuela, M.D.; Moreno-Bondí, M.C.; Orellana, G.; Langmuir, 1999, 15, 6451; García-Fresnadillo, D.; Tesis Doctoral, Universidad Complutense de Madrid, Madrid, 1996] supports, embedment for poly(vinyl chloride) membranes [Bakker, E.; Bühlmann, P.; Pretsch, E.; Chem.Rev. 1997, 97, 3083; Seiler, K.; Simon, W.; Anal.Chim. Acta, 1992, 266, 73; Seiler, K.; in "Ion-Selective Optode Membranes"; Fluka Chemie A.G., Buchs, Suiza, 1993 (Fluka N° 58166); Morf, W.E.; Seiler, K.; Lehman, B.; Behringer,

Ch.; Hartman, K.; Simon, W.; Pure Appl. Chem. 1989, 61, 1613; Eugster, K.; Rosatzin, T.; Rusterholz, B.; Aebersold, B.; Pedrazza, V.; Rüegg, D.; Schmid, A.; Spichiger, U.; Simon, W.; Anal. Chim. Acta. 1994, 289, 1; Okada, T.; Sugihara, H.; Hiratani, K.; Analyst, 1995, 120, 2381] and silicic sol-gel materials [Lev, O.; Tsionsky, M.; Rabinovich, L.; Glezer, V.; Sampath, S.; Pankratov, I.; Gun, J.; Anal. Chem. 1995, 67, 22A; Avnir, D.; Levy, D.; Reisfeld, R.; J. Phys. Chem. 1984, 88, 5956; Aylott, J.W.; Richardson, D.J.; Russell, D.A.; Chem. Mater. 1997, 2, 2261; Habilo Jiwan, J.-L.; Soumil-
 5 lion, J.-Ph.; J. Non-Cryst. Solids 1997, 220, 316; Wallington, S. A.; Pilon, C.; Wright, J.D.; J. Sol-Gel Sci. Tech. 1997, 8, 1127; Isoefzon-Kuyasuskava, B.; Gigozin, I.; Ottolenghi, M.; Avnir, D.; Lev, O.; J. Non-Cryst. Solids 1992, 147, 808; Klein, L.C. in Sol-Gel Optics: Processing and Applications, Kluwer Academic Publisher, Norwell, MA, 1994] and covalent binding for silicagel [Locke, D.C.; J. Chromatographic Sci. 1973, 11, 120; Brust, O.E.; Sebastian, I.; Halasz, I.; J. Chro-
 10 matography 1973, 83, 15; Locke, D.C.; Schmerru, J.T.; Banner, B.; Anal. Chem. 1971, 60, 329; Yam, C.M.; Kakkar, A.K.; J. Chem. Soc., Chem. Commun. 1995, 907], porous glass [Locke, D.C.; J. Chromatographic Sci. 1973, 11, 120; Brust, O.E.; Sebastian, I.; Halasz, I.; J. Chromatography 1973, 83, 15; Locke, D.C.; Schmerru, J.T.; Banner, B.; Anal. Chem. 1971, 60, 329; Xavier, M.P.; García-Fresnadillo, D.; Moreno-Bondi, M.C.; Orellana, G.; Anal. Chem. 1998, 70, 5184; Basile, L.A.; Barton, J.K.; J. Am. Chem. Soc. 1987, 109, 7458; Howells, R.D.; McCown, D.J.; Chem. Rev. 1977,
 15 77, 69; Efferberger, K.; Huthnacher, K.; Angew. Chem. Int. Ed. Engl. 1974, 13, 409] and styrene copolymers [Arnold, M.A.; Anal. Chem. 1992, 64, 1015A; Frechet, J. M. J.; Farrall, M. J.; in The Chemistry and Properties of Crosslinked Polymers, (S.S. Labana, ed.), Academic Press, New York, 1977; p.59; Neckers, D.C.; Kooistra, D.A.; Green, G.W.; J. Am. Chem. Soc. 1972, 94, 9284].

[0022] The indicator chemistry of the sensors disclosed in this invention can be classified, according to the type of interaction between the analyte and the reactive phase, as formation of a complex (for example with the couples 5-hydroxy-1,10-phenanthroline/silicagel, sodium 1,10-phenanthroline-4,7-di(phenylsulphonate) / porous glass, 1,10-phenanthroline/silicic sol-gel materials, 1,10-phenanthroline/Nafion® and vinyl-phenanthroline/styrene-divinyl-
 20 benzene) or an acid-base reaction (for example N-[2-(4-hydroxybenzyl)phenyl]-2,2-dimethylpropanamide/silicagel, N-(2-benzylphenyl)perfluorooctanamide/polytetrafluoroethylene, 5-perfluorooctanamide-1,10-phenanthroline/
 25 Nafion® and triphenylmethane/Amberlite®).

[0023] The sensor according to the invention is stable within a range of temperature that is characteristic of the support/indicator system. If the sensor is not stable at the reaction temperature, it is possible to locate the sensor in a thermostated loop, maintained in constant circulation with the reactor or medium where the polymerization or organic reaction takes place.

[0024] The sample to be analysed comprises a solution of the organometallic to be determined in a suitable solvent.

[0025] The sensor according to the present invention may be used for the qualitative and/or quantitative determination of organometallic compounds, specially organometallic compounds wherein the metal is a metal of groups 1, 2 or 13 of the Periodic Table of the Elements, in, for example, industrial and laboratory chemical synthesis. In a particular embodiment, the sensor according to the present invention is useful for the determination of the neutralization point of all impurities that destroy the organolithium initiator in anionic polymerization processes or any other chemical re-
 35 action that involves an organolithium compound in an organic medium.

[0026] Another object of the present invention is the method, based on the use of an optical sensor, useful for determining organolithium compounds and particularly for determining the reaction threshold in the anionic polymerization of a 1,3-conjugated diene and/or monoalkenyl aromatic hydrocarbon copolymer initiated by organolithium compounds or any other reaction that involves an organometallic compound being critical the stoichiometry of the same.

[0027] The method comprises contacting the sensor according to the present invention with the sample to be analysed under conditions wherein the indicator reversibly reacts with the organometallic compound to render a reaction product having a characteristic absorption, reflectance or emission band in the range between 150 nm and 15000 nm, and measuring the absorption, reflectance or emission of the functionalized support at the characteristic wavelength and transforming it in the concentration of the organometallic compound present in the solution.

[0028] In a particular embodiment, the method for the determination of the concentration of organometallic compounds is characterized by the on-line use of a sensor according to the present invention, the sensor being located in a thermostated loop, maintained in constant circulation with the reactor and the measurement being made directly in the reaction medium.

[0029] The method may be applied for the determination of the neutralization point of all the existing impurities that can destroy the organometallic initiator in the anionic polymerization of a 1,3-conjugated diene and/or monoalkenyl aromatic hydrocarbon copolymer initiated by organolithium compounds. The method may also be applied for the de-
 50 termination of organometallic compounds in industrial and laboratory chemical synthesis.

EXAMPLES**EXPERIMENTAL METHOD**

[0030] All the tests which are described in the present invention were carried out in a polymerization reactor with a capacity of 1 or 20 liters, provided with conditioning systems for nitrogen, venting and thermostating. Although it is possible to work in a continuous or semicontinuous mode, in this case a batch operation was used, i.e. a discontinuous mode. Raw materials were purified using the methods described in the state of the art (for example distillation, drying, etc.).

Example 1

[0031] This example corresponds to the determination of *n*-butyllithium using a fiber-optic sensor according to the object of the invention.

[0032] The fiber-optic sensor is composed by the following elements:

- Indicator: N-[2-(4-hydroxybenzyl)phenyl]-2,2-dimethylpropanamide (HBPD). This indicator dye is prepared: firstly according to the general procedure of aromatic amines *o*-functionalization described by Fuhrer and Gschwend [Fuhrer, W.; Gschwend, H.W.; J.Org.Chem. 1979, 44, 1133; Gschwend, H.W.; Rodríguez, H.R.; Org. React. 1979, Vol.26], secondly, the nitrocompound is reduced with hydrazine monohydrate using the method described by Nasielski-Hinkens et al. [Nasielski-Hinkens, R.; Benedeck-Vamos, M.; Maetens, D.; J.Heterocycl. Chem. 1980, 17, 873]; finally, the diazonium salt is prepared using sodium nitrite and sulphuric acid and then is neutralized with sulphuric acid in water, obtaining the phenol.
- Support: Silica gel
- Immobilization procedure: Covalent. The method followed to functionalize silicagel supports is based on the matrix surface chemical modification with amine-Si or amine-Sn groups [Yam, C.M.; Kakkar, A.K.; J. Chem. Soc., Chem. Commun. 1995, 907] [Fessenden, R.; Fessenden, J. S.; Chem. Rev. 1961, 61, 361] [Jones, K.; Lappert, M. F.; in "Organotin Compounds", Vol.2, Ed. A.K. Sawyer, Marcell Dekker, Inc., New York, 1977; p.150]. These groups will let us bind the different cromophores to the support with an stable, for example in anionic polymerization conditions, ether bond.
- Measurement principle: Reflectance

[0033] Once the sensitive terminal is prepared, by placing it at the distal end of a fiber-optic, it was introduced into the sample solution or reaction medium. The method consists in the addition of different aliquots of *n*-butyllithium (i.e. 1.6 M in cyclohexane solution) into a closed and nitrogen inertized reaction vessel with the sample to titrate, up to the detection of chromophore species, monitored by an spectrophotometer connected to the fiber-optic.

[0034] Figure 1 shows the variation of the Kubelka-Munk reflectance function, $F(R)$, of the HBPD immobilized on silica gel, as a function of the final *n*-butyllithium concentration added.

[0035] As it is shown in figure 1, there is not reflectance observed if no *n*-butyllithium is added (— 0 M *n*-BuLi, reference baseline). Subsequently, the presence of species existing in the reaction medium that can kill the *n*-butyllithium does not allow the appearance of any reflectance in the spectra up to a concentration of 1.58×10^{-2} M of added *n*-butyllithium (— 1.58×10^{-2} M *n*-BuLi) with the appearance of a maximum $F(R)$ at 370 nm. This maximum value is associated to full reaction of the immobilized indicator (HBPD) with the active *n*-butyllithium, that remains after the stoichiometric neutralization of all the poisons.

[0036] This could be the control starting point from which all the *n*-butyllithium added would act as active initiator of anionic polymerization or other reaction that involves this kind of compounds.

[0037] Figure 1 also shows that after addition of a known ammount of *n*-butanol (..... 5.3×10^{-2} M *n*-BuOH, in figure 1) the complex is destroyed, reflectance of initial base line is recovered and the sensitive terminal can be used again.

[0038] According to the procedure described above, the determination of the concentration of an unknown solution of *n*-butyl-lithium can be performed by introducing a known amount ("A" mol) of an alcohol (e.g. *n*-butyl alcohol) as a proton donor into the inertized solvent where the optical sensor is placed. In this moment, the unknown *n*-butyl-lithium solution is added up to the point where the established criterion value of reflectance at 370 nm is achieved. The amount of *n*-butyllithium added ("C" milliliters of *n*-butyllithium solution) is equivalent to the known amount of *n*-butyl alcohol in mol. Therefore, the concentration of *n*-butyllithium in mol/l is calculated as:

$$\text{Concentration of the } n\text{-butyllithium solution (mol/l)} = (A \times 64000) / C$$

Example 2

[0039] This example corresponds to the determination of *n*-butyllithium using a fiber-optic sensor according to the object of the invention.

[0040] The fiber-optic sensor is composed by the following elements:

- Indicator: Triphenylmethane (TPM)
- Support: Highly crosslinked styrene-divinyl benzene copolymer (Amberlite® XAD-2).
- Immobilization procedure: Covalent. The functionalization of styrene divinylbenzene copolymers is based on Friedel-Crafts alkylation of the polymer with diphenylmethyl chloride through the $AlCl_3$ complex in nitrobenzene [Neckers, D.C.; Kooistra, D.A.; Green, G.W.; J. Am. Chem. Soc. 1972, 94, 9284; Obrecht, D.; Villaigordo, J. M.; "Solid-Supported Combinatorial and Parallel Synthesis of Small Molecular Weight Compounds Libraries" in "Tetrahedron Organic Chemistry Series", Vol. 17, Pergamon Press, Oxford, 1998; Cap.1, pp. 28-45; Cohen, B. J.; Kraus, M. A.; Patchornik, A.; J. Am. Chem. Soc. 1981, 103, 7620; Cohen, B. J.; Kraus, M.A.; Patchornik, A.; J. Am. Chem. Soc. 1977, 99, 4165]
- Measurement principle: Reflectance

[0041] Once the sensitive terminal is prepared, by placing it at the distal end of a fiber-optic, it was introduced into the sample solution or reaction medium. The method consists in the addition of different aliquots of *n*-butyllithium (e.g. 1.6 M in cyclohexane solution) into a closed and nitrogen inertized reaction vessel with the sample to titrate, up to the detection of chromophore species, monitored by an spectrophotometer connected to the fiber optic.

[0042] Figure 2 shows the response of triphenylmethane covalently bound to Amberlite® XAD-2, at 25°C after addition of *n*-butyllithium following the procedure of aliquots addition.

[0043] As it is shown in figure 2, there is not reflectance observed if no *n*-butyllithium is added (—0 M *n*-BuLi, reference baseline). Subsequently, the presence of species existing in the reaction medium that can kill the *n*-butyllithium does not allow the appearance of any reflectance in the spectra up to a concentration of 2.75×10^{-2} M of added *n*-butyllithium (— 2.75×10^{-2} M *n*-BuLi), showing a characteristic spectra of the chromophore formed by reaction of active *n*-butyllithium and the sensitive terminal, associated with triphenyl methane deprotonation. The reflectance value observed at 450 nm is taken as the control criteria, that represents the complete reaction of indicator and active *n*-butyllithium, being constant once the full neutralization of impurities or "poisons" is effective.

[0044] This could be the control starting point from which all the *n*-butyllithium added would act as active initiator of anionic polymerization or other reaction that involves this kind of compounds.

[0045] Figure 2 also shows that after addition of a known amount of *n*-propanol (..... 5.3×10^{-2} M *n*-PrOH, in figure 2) the complex is destroyed, reflectance of initial base line is recovered and the sensitive terminal can be used again.

[0046] According to the procedure described above, the determination of the concentration of an unknown solution of *n*-butyl-lithium can be performed by introducing a known amount ("A" mol) of an alcohol (e.g. *n*-propyl alcohol) as a proton donor into the inertized solvent where the optical sensor is placed. In this moment, the unknown *n*-butyl-lithium solution is added up to the point where the established criterion value of reflectance at 450 nm is achieved. The amount of *n*-butyllithium added ("C" milliliters of *n*-butyllithium solution) is equivalent to the known amount of *n*-propyl alcohol in mol. Therefore, the concentration of *n*-butyllithium in mol/l is calculated as:

$$\text{Concentration of the } n\text{-butyllithium solution (mol/l)} = (A \times 64000) / C$$

Example 3

[0047] This example corresponds to homopolymerization of styrene with the previous reaction threshold determination using a fiber-optic sensor according to the object of the invention before the monomer and initiator addition to the reactor.

[0048] The fiber-optic sensor consists of the following elements:

- Indicator: Sodium 1,10-phenanthroline-4,7-di(phenylsulphonate) (S2D)
- Support: Commercially available porous glass (PG) with different pore size containing γ -aminopropyl groups on its surface.
- Immobilization procedure: Covalent [Xavier, M.P.; García-Fresnadillo, D.; Moreno-Bondi, M.C.; Orellana, G.; Anal. Chem. 1998, 70, 5184; Basile, L.A.; Barton, J.K.; J. Am. Chem. Soc. 1987, 109, 7458; Howells, R.D.; McCown, D. J.; Chem. Rev. 1977, 77, 69; Efferberger, K.; Huthnacher, K.; Angew. Chem. Int. Ed. Engl. 1974, 13, 409]. The indicator attachment requires (i) preparation of the sulphonyl bromide and (ii) formation of a mixed anhydride with

silver trifluoromethanesulphonate. In a second step, the reaction between the amino groups present in the porous glass and the anhydride yields the sulphonamide.

- Measurement principle: Reflectance

[0049] Once the sensitive terminal is prepared, by placing it at the distal end of a fiber-optic, it was introduced into the reaction medium. In the first step, 800 ml of cyclohexane are added to the reactor (1 liter capacity) and then it is thermostated at 40 °C under stirring. Once the target temperature is reached, the reflectance spectrum of cyclohexane is collected as a reference. Subsequently, different aliquots of a cyclohexane solution of *n*-butyllithium (3% by weight) are added and, at the same time, the reflectance spectra of the different coloured species formed by the indicator (optical sensor) and *n*-butyllithium are collected in order to determine the reaction threshold.

[0050] Once the reaction threshold is determined, a cyclohexane solution of styrene is added and then *n*-butyllithium in stoichiometric amount required to initiate the styrene polymerization and obtaining the target molecular weight. The reaction is allowed to proceed adiabatically, with a slight increase in temperature. Confirmed the absence of styrene, the living polymer chains are terminated with a proton donor such as an alcohol.

[0051] In figure 3, we can see the variation of the reflectance of the sensitive terminal based on S2D/PG during the threshold determination and during the first stage of styrene polymerization ($[\text{Styrene}]_0 = 0.65 \text{ M}$) in cyclohexane, initiated by *n*-butyllithium. The first decrease at $R_{600\text{nm}}(\%)$ (it is possible also to use other wavelengths, i.e. $R_{700\text{nm}}$ and $R_{450\text{nm}}$) is associated with the neutralization of all impurities existing in the reactor (in this case, figure 3, approximately at 7 minutes of experiment record). The second step in the basal reflectance of the sensitive terminal (in this case, figure 3, above 15 minutes of experiment record) is associated with the addition of the monomer and *n*-butyllithium that will initiate the polymerization in the required amount to reach the molecular weight target.

[0052] Then, the peak molecular weight and the molecular weight distribution was determined by gel permeation chromatography based on a calibration curve of polystyrene standards, obtaining a polydispersity ratio M_w/M_n of 1.07, molecular weight peak 48000 (target 50000), showing a good fit of molecular weight after determination of the reaction threshold using this optical sensor.

Example 4

[0053] This example corresponds to a medium molecular weight styrene homopolymerization with the previous reaction threshold determination and repeatability study using an optical fiber sensor in the presence of monomer according to the object of the invention.

[0054] The active optic fiber sensor is composed by the following elements:

- Indicator: 1,10-phenanthroline (PHEN)
- Support: Plasticized poly(vinyl chloride) membranes (PVC).
- Immobilization procedure: Embedding (physically entrapped). The membrane [Seiler, K.; "Ion-Selective Optode Membranes"; Fluka Chemie A.G., Buchs, Suiza, 1993 (Fluka Pub. No. 58166)] contains 1,10-phenanthroline as ligand and *n*-butyllithium titration reagent, a plasticizer [Eugster, K.; Rosatzin, T.; Rusterholz, B.; Aebersold, B.; Pedrazza, V.; Rüegg, D.; Schmid, A.; Spichiger, U.; Simon, W.; Anal.Chim.Acta. 1994, 289, 1; Okada, T.; Sugihara, H.; Hiratani, K.; Analyst, 1995, 120, 2381] (bis-(2-ethylhexyl) sebacate (DOS)) and an anionic additive (potassium tetrakis-(4-chlorophenyl)borate (KTCBP)). All the chemicals are well dissolved in tetrahydrofuran and placed in a Petri plate. Once the solvent is eliminated at room temperature, a 100 µm thick membrane is obtained.
- Measurement principle: Absorbance

[0055] The sensitive terminal is prepared by placing the membrane sensor, obtained according above procedure, at the distal end of a fiber optic.

[0056] The experiments are performed in a 20 liter capacity reactor provided with an external recirculation loop with a heat-exchanger. The sensitive terminal is located in the external loop in order to make the threshold determination at the optimum measurement temperature. This is the way to keep the reactor at 60 °C (polymerization temperature) and the sensor in the external loop at 30 °C.

[0057] In the first step, 9.5 liter of cyclohexane and 5.1 liter of a cyclohexane solution of styrene (25% by weight) are added to the reactor and then it is thermostated to 60 °C under stirring, while the external loop temperature is kept at 30 °C. Once the temperature is reached, the absorption spectrum of cyclohexane and styrene is recorded as a reference. Subsequently, different aliquots of a cyclohexane solution of *n*-butyllithium (3% by weight) are added and, at the same time, are continuously collected absorption data at 350 nm (similar results are obtained at other wavelengths, e. g. 400 nm, 470 nm and 520 nm) in order to determine the reaction threshold (see figure 4).

[0058] Once the reaction threshold is determined, what is shown by sharp slope change in absorbance data at any of the wavelengths indicated above (in this case at about 7 minutes of experiment record, see figure 4), a cyclohexane

solution of *n*-butyllithium 3% (by weight) is added to initiate the polymerization of styrene in stoichiometric amount to obtain a target molecular weight of 50000 g/mol. Then, the reaction is allowed to continue adiabatically, with a slight increase in temperature. Confirmed the absence of styrene, the living polymer chains are terminated with a proton donor such as an alcohol and consequently, the absorbance values will drastically decrease because of the disappearance of the reactive species and the charge transfer complex formed in the sensitive terminal (see figure 4, in this cases at about 55 minutes of experiment record).

[0059] Then, the peak molecular weight and the molecular weight distribution were determined by gel permeation chromatography based on a calibration curve of polystyrene standards.

[0060] These experiments were repeated ten times, with the same sensor, where different aliquots of an alcohol as a poisson of *n*-butyllithium were added on each reaction, such as to produce a relative standard deviation of 35% over target molecular weight. Nevertheless, through the application of threshold determination methodology described above, molecular weight obtained showed a good repeatability. The molecular weight distributions are, in all cases, unimodal and the variability of the molecular weight of the obtained polymers (Relative Standard Deviation) is lower than 7%, in contrast with the higher value of 35% for styrene polymerization in case of no control of reaction threshold was used.

Example 5

[0061] This example corresponds to a high molecular weight styrene homopolymerization with the previous reaction threshold determination and repeatability study using an optic fiber sensor in presence of the monomer according to the object of the invention.

[0062] The fiber-optic sensor is composed by the following elements:

- Indicator: 1,10-phenanthroline (PHEN)
- Support: Polyvinyl chloride membranes (PVC).
- Immobilization procedure: Embedding (physically entrapped)
- Measurement principle: Absorbance

[0063] The sensitive terminal is prepared by placing the membrane sensor at the distal end of a fiber-optic, obtained according to the above procedure described in example 4. The experiments are performed in a 20 liter capacity reactor provided with a external recirculation loop with a heat-exchanger. The sensitive terminal is located into the external loop in order to make the threshold determination at the optimum measurement temperature. This is the way to keep the reactor at 60 °C (polymerization temperature) and the sensor in the external loop at 30 °C.

[0064] In the first step, 9.6 liter of cyclohexane and 5.1 liter of a cyclohexane solution of styrene (25% by weight) are added to the reactor and then it is thermostated to 60 °C under stirring, while the external loop temperature is kept at 30 °C. Once the temperature is reached, the absorption spectrum of cyclohexane and styrene is recorded as a reference. Subsequently, different aliquots of a cyclohexane solution of *n*-butyllithium (3% by weight) are added and, at the same time, are continuously collected absorption data at 350 nm (similar results are obtained at other wavelengths, e.g. 400 nm, 470 nm and 520 nm) in order to determine the reaction threshold (see figure 5).

[0065] Once the reaction threshold is determined, what is shown by sharp slope change in absorbance data at any of the wavelengths indicated above (in this case at about 8 minutes of experiment record, see figure 5), a cyclohexane solution of *n*-butyllithium 3% (by weight) is added to initiate the polymerization of styrene in stoichiometric amount to obtain a target molecular weight of 140000 g/mol. Then, the reaction is allowed to continue adiabatically, with a slight increase in temperature. Confirmed the absence of styrene, the living polymer chains are terminated with a proton donor such as an alcohol and consequently, the absorbance values will drastically decrease because of the disappearance of the reactive species and the charge transfer complex formed in the sensitive terminal (in this case, see figure 5, at about 40 minutes of experiment record).

[0066] Then, the peak molecular weight and the molecular weight distribution were determined by gel permeation chromatography based on a calibration curve of polystyrene standards.

[0067] These experiments were repeated ten times, with the same sensor, where different aliquots of an alcohol as a poisson of *n*-butyllithium were added on each reaction, such as to produce a relative standard deviation of 120% over target molecular weight. Nevertheless, through the application of threshold determination methodology described above, molecular weight obtained showed a good repeatability. The molecular weight distributions are, in all cases, unimodal and the variability of the molecular weight of the obtained polymers (Relative Standard Deviation) is lower than 7%, in contrast with the higher value of 120% for styrene polymerization in case of no control of reaction threshold was used.

Claims

1. Sensor for the qualitative and/or quantitative determination of organometallic compounds comprising the following elements:

a. an inorganic, organic or polymeric support, insoluble in the sample to analyze;
 b. an indicator which reversibly reacts with the organometallic compound and whose reaction product gives a characteristic absorption, reflectance or emission band in the range 150-15000 nm and which is physically trapped, adsorbed, absorbed, dissolved or chemically linked in an electrostatic or covalent way to the support, and
 c. an optical sensor which measures the absorption, reflectance or emission of the functionalized support at the characteristic wavelength and transforms it in the concentration of the organometallic compound present in the solution.

2. Sensor according to claim 1, wherein the indicator is selected from the group consisting of 1,10-phenanthroline, 5-amino-1,10-phenanthroline, 5-nitro-1,10-phenanthroline, 4,7-dimethyl-1,10-phenanthroline, 4,7-diphenyl-1,10-phenanthroline, 5-hydroxy-1,10-phenanthroline, sodium 1,10-phenanthroline-4,7-di(phenylsulphonate), 5-perfluorooctanamide-1,10-phenanthroline, 4-vinyl-7-methyl-1,10-phenanthroline, N-(2-methyl)-2,2-dimethylpropanamide, N-[2-(4-hydroxybenzyl)phenyl]-2,2-dimethylpropanamide, N-(2-benzylphenyl)perfluorooctanamide, N-[4-(2-(2,2-dimethylpropanoylamine)benzyl)phenyl]perfluorooctanamide, 4,4'-(difluorophenyl)phenylmethane and triphenylmethane.

3. Sensor according to claim 1 or 2 wherein the support is selected from silicagel, powdered porous glass, porous glass layer, polydimethylsiloxanes, silicic xerogels, polytetrafluoroethylene, polyvinyl chloride, Nafion® membranes and styrene-divinyl benzene copolymers.

4. Sensor according to claims 1 to 3, wherein the metal of the organometallic compound is a metal of group 1, 2 or 13 of the Periodic Table of the Elements.

5. Sensor according to claim 4, wherein the metal is lithium

6. Sensor according to claims 1-5, wherein the characteristic band of the indicator is in the range between 200 and 800 nm.

7. Sensor according to claim 1, wherein the indicator is 1,10-phenanthroline or a derivative thereof, the support is poly(vinylchloride) (PVC) and the indicator is immobilized on the support by physical entrapment.

8. Sensor according to claim 1, for the determination of the neutralization point of all the impurities that destroy the organolithium initiator in anionic polymerization processes or any other chemical reaction that involves an organolithium compound in an organic medium.

9. Method for the determination of the concentration of organometallic compounds **characterized by** the on-line use of a sensor according to any claims 1 to 8.

10. Method according to claim 9, wherein the sensor is located in a thermostated loop, maintained in constant circulation with the reactor.

11. Method according to claim 9, wherein the measurement is made directly in the reaction medium.

12. Method according to claim 9, for the determination of the neutralization point of all the existing impurities that can destroy the organometallic compound.

13. Method according to claim 9, for the determination of organometallic compounds in industrial and laboratory chemical synthesis.

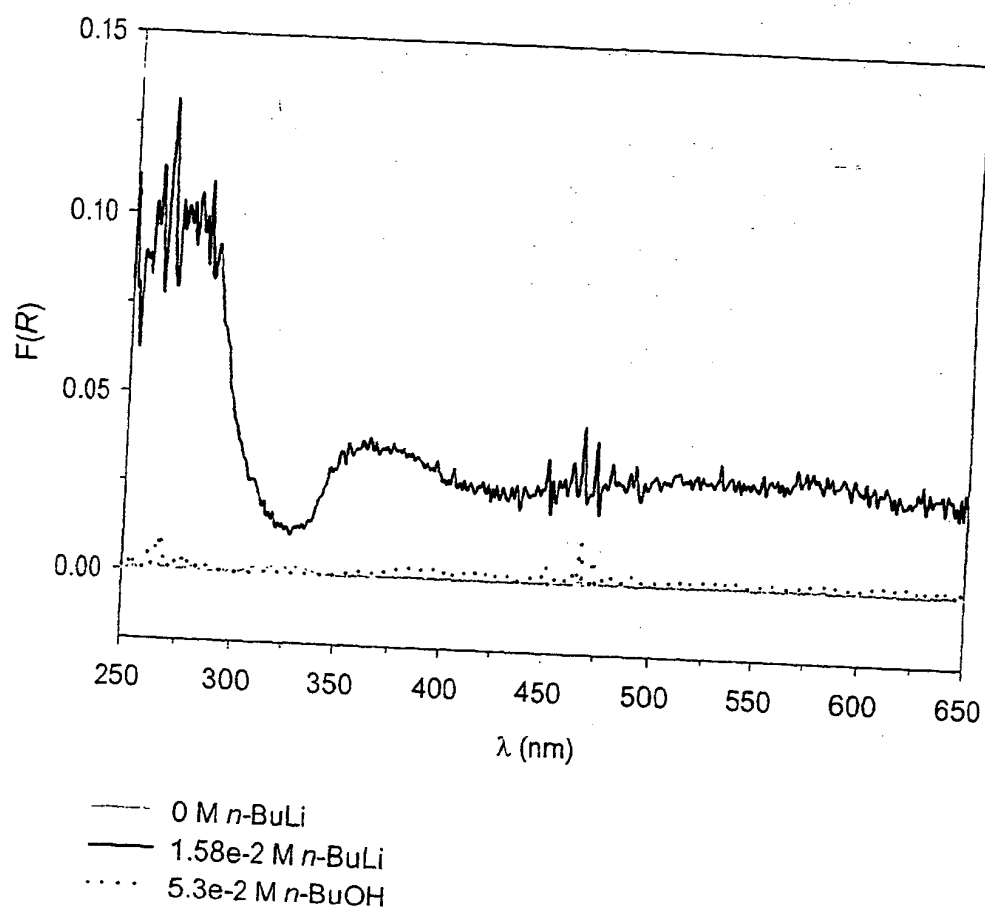


Figure 1

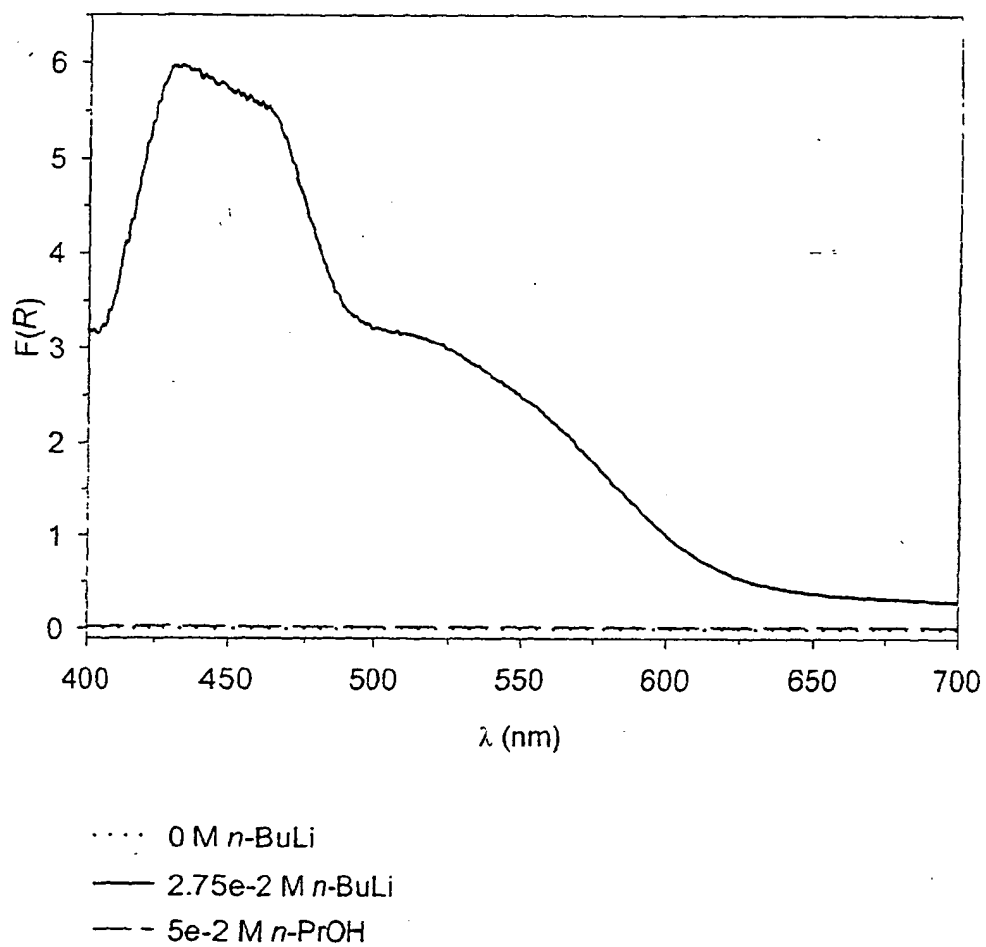


Figure 2

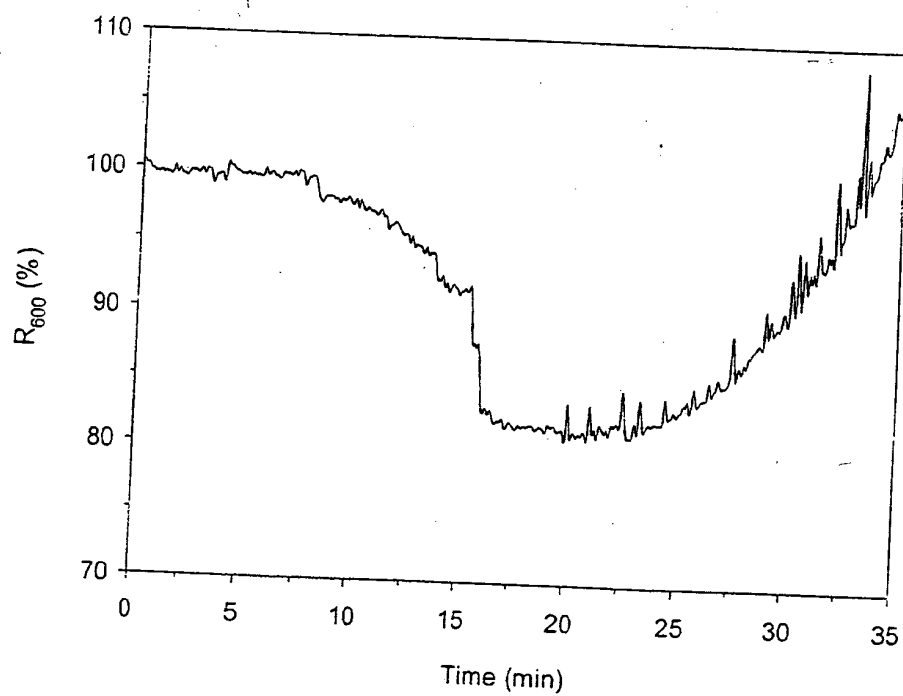


Figure 3

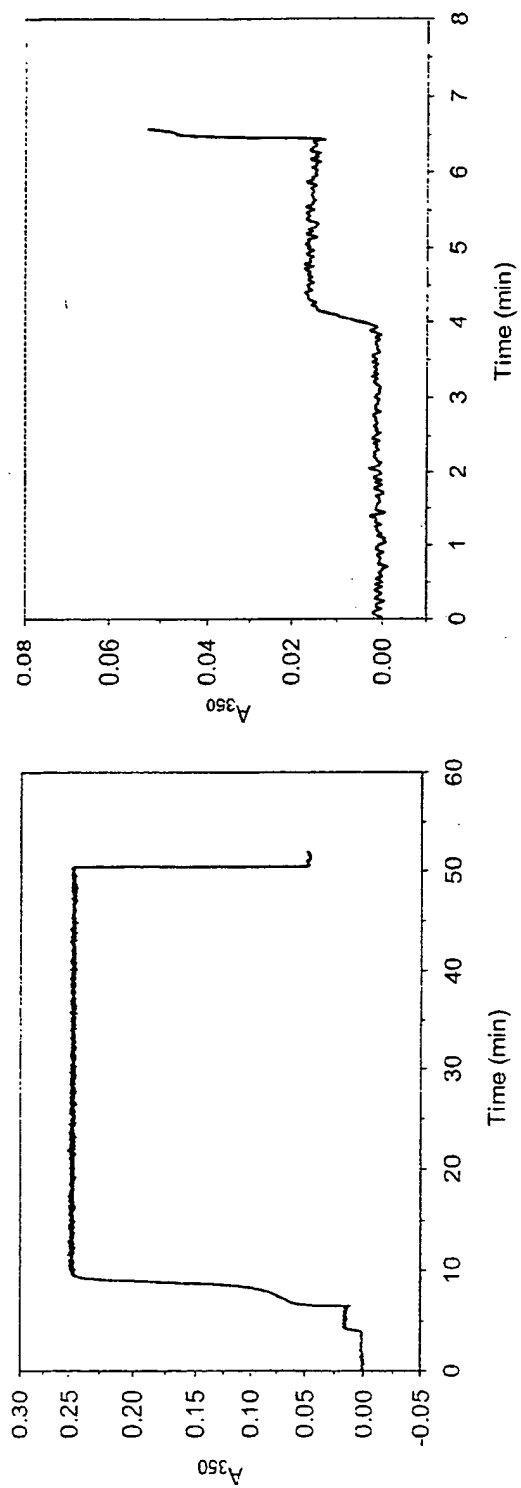


Figure 4

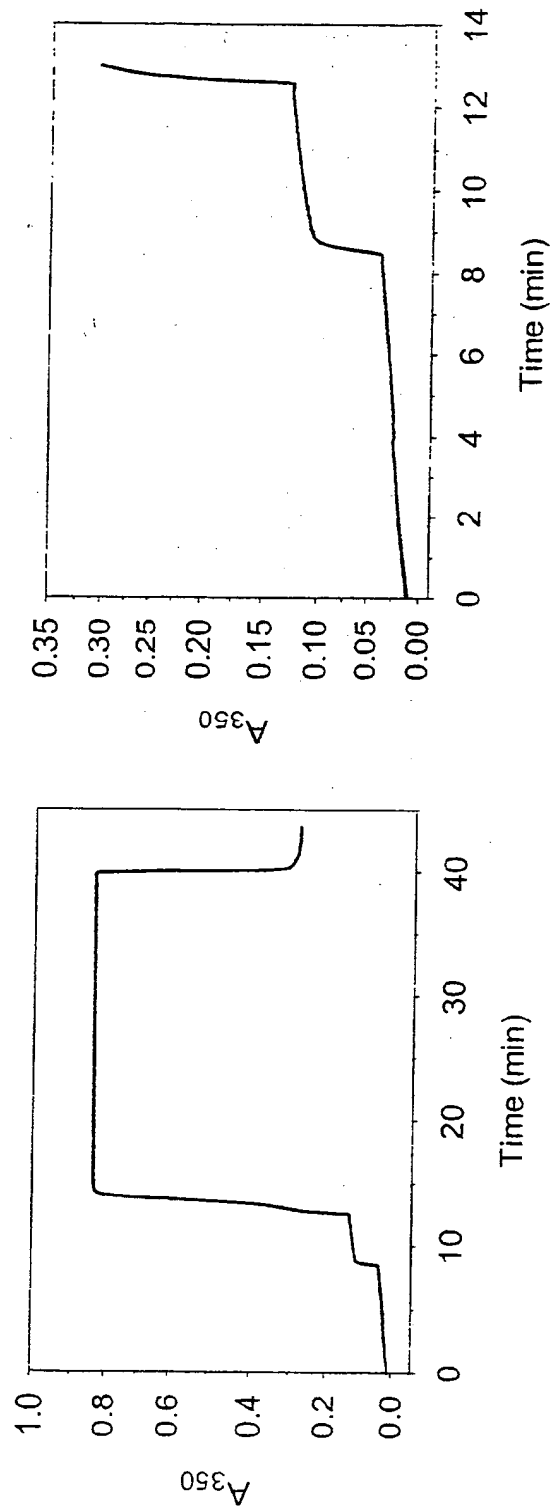


Figure 5



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which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

EP 01 50 0101

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	US 5 212 099 A (MARCUS M A) 18 May 1993 (1993-05-18)	1-7	G01N21/77
Y	* column 1, line 17 - column 2, line 31; column 4, line 49 - column 5, line 12; figures 1,5 *	8-13	
D,A	WATSON S C ET AL: "Colored indicators for simple direct titration of magnesium and lithium reagents" JOURNAL OF ORGANOMETALLIC CHEMISTRY, vol. 9, 1967, pages 165-168, XP001021700 ISSN 0022-328X * the whole document *	1,2,4-7	
			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			G01N
INCOMPLETE SEARCH			
<p>The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims.</p> <p>Claims searched completely:</p> <p>Claims searched incompletely:</p> <p>Claims not searched:</p> <p>Reason for the limitation of the search:</p> <p>see sheet C</p>			
Place of search		Date of completion of the search	Examiner
MUNICH		4 October 2001	Johnson, K
CATEGORY OF CITED DOCUMENTS			
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EPO FORM 1503 03 82 (P4/G07)

European Patent
OfficeINCOMPLETE SEARCH
SHEET CApplication Number
EP 01 50 0101Claim(s) searched incompletely:
1-13

Reason for the limitation of the search:

Present claim 1 relates to a sensor for determining an arbitrary organometallic compound, ie a vast range of compounds. Moreover the subject matter of the claim is defined in terms of desirable characteristics or properties of the indicator composition employed in the sensor. Thus the indicator reacts reversibly with the organometallic compound to yield a reaction product which has a characteristic absorption, reflectance or emission band in the range 150-150000 nm., ie. virtually anywhere in the electromagnetic spectrum. So the claim seeks protection for sensors including any indicator having these properties. In contrast, the application provides support within the meaning of Article 84 EPC for only a very limited number of embodiments. Indeed, only embodiments in which the analyte is n-butyllithium are described. Moreover, it must be doubted that the indicator compositions specified in the preferred embodiments, and in particular in claim 2, possess these attributes for all organometallic compounds, whatever the composition of the latter. At any rate, there are no grounds to believe that they can be employed successfully across the whole scope of the invention. Therefore the claim so lacks support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Consequently, the search has been restricted to fibre optical sensors for the determination of alkylmetal compounds of Groups 1 and 2 of the Periodic Table, which comprise the indicator compositions disclosed in examples 1-5, namely
N-(2-(4-hydroxybenzyl)phenyl)-2,2-dimethylpropanamide, trimethylmethane, sodium 1,10-phenanthroline-4,7-di(phenylsulphonate), and 1,10-phenanthroline.

Claims 2-13 were only searched insofar as they describe preferred embodiments of this subject matter.

Application Number

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
Y	<p>DATABASE CHEMABS 'Online! Chemical Abstracts Services, Columbus, Ohio, US; XU Y ET AL: "On-line determination method and determination instrument of impurity removal end point of lithium system polymerization" retrieved from STN Database accession no. 132:308844 XP002177759 * abstract * & CN 1 216 368 A (INST YANSHAN PETRO-CHEM CORP BEIJING) 12 May 1999 (1999-05-12) -& DATABASE WPI Section Ch, Week 9937 Derwent Publications Ltd., London, GB; Class A18, AN 1999-431069 XP002177760 & CN 1 216 368 A (...), 12 May 1999 (1999-05-12) * abstract *</p>	8-13	<p>TECHNICAL FIELDS SEARCHED (Int.Cl.7)</p>
Y	<p>US 5 650 331 A (JORGENSEN B S ET AL) 22 July 1997 (1997-07-22) * column 3, line 27 - column 4, line 49; column 5, line 55 - column 6, line 62; figures 1,3 *</p>	1-6	
D,Y	<p>EPPLEY R J ET AL: "Quantitative analysis of organolithium reagents" JOURNAL OF ORGANOMETALLIC CHEMISTRY, vol. 8, 1967, pages 176-178, XP001018099 ISSN 0022-328X * the whole document *</p>	1-6	



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Application Number

EP 01 50 0101

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A	US 3 290 116 A (CARROLL J H) 6 December 1966 (1966-12-06) * column 2, line 32 - column 4, line 60; figure *	1,2,4-6; 8-13	
A	US 5 656 241 A (SEIFERT K R ET AL) 12 August 1997 (1997-08-12) * column 6, line 3 - column 8, line 34; column 13, lines 21-40; figures 1-5 *	1-3,6,7	
A	ES 2 134 122 A (UNIVERSIDAD COMPLUTENSE DE MADRID) 16 September 1999 (1999-09-16) * claim 7; example *	1-3,6,7	
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**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 01 50 0101

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04-10-2001

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